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(51) International Patent Classification ⁷ : C07K 7/50, A61K 38/12	A3	(11) International Publication Number: WO 00/11023 (43) International Publication Date: 2 March 2000 (02.03.00)
(21) International Application Number: PCT/US99/18908 (22) International Filing Date: 18 August 1999 (18.08.99) (30) Priority Data: 60/097,228 20 August 1998 (20.08.98) US (71) Applicant (for all designated States except US): ELI LILLY AND COMPANY [US/US]; Lilly Corporate Center, Indianapolis, IN 46285 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): BORROMEO, Peter, Stanley [US/US]; 10783 Thistle Ridge, Fishers, IN 46038 (US). COHEN, Jeffrey, Daniel [US/US]; 1411 Shawnee Road, Indianapolis, IN 46260 (US). GREGORY, George, Stuart [US/US]; 6295 Valleyview Drive, Fishers, IN 46038 (US). HENLE, Stacy, Kay [US/US]; 1220 East Polk Street, Indianapolis, IN 46202 (US). HITCHCOCK, Stephen, Andrew [GB/US]; 1484 Stormy Ridge Court, Carmel, IN 46032 (US). JUNGHEIM, Louis, Nickolaus [US/US]; 8218 Meadowbrook Drive, Indianapolis, IN 46240 (US). MAYHUGH, Daniel, Ray [US/US]; 9681 Troon Court, Carmel, IN 46032 (US). SHEPHERD, Timothy, Alan [US/US]; 8463 Slippery Elm Court, Indianapolis, IN 46227 (US). TURNER,		William, Wilson, Jr. [US/US]; 4000 Saratoga Drive, Bloomington, IN 47408 (US). (74) Agents: LEHNHARDT, Susan, K. et al.; Morrison & Foerster LLP, 1290 Avenue of the Americas, New York, NY 10104-0012 (US). (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> (88) Date of publication of the international search report: 15 June 2000 (15.06.00)
(54) Title: RING MODIFIED CYCLIC PEPTIDE ANALOGS		
(57) Abstract <p>A method for modifying the cyclic peptide ring system of Echinocandin-type compounds to produce new analogs having antifungal activity is provided. The inventive process comprises opening the cyclic peptide ring, cleaving the terminal ornithine unit, inserting at least one new amino acid or other synthetic unit and closing the ring to produce a new cyclic peptide ring structure. The process allows one to incorporate features such as water-solubility into the cyclic peptide ring nucleus, sites for further modification, increase or decrease the number of amino acid or peptide units within the ring nucleus, and increase or decrease the total number of members within the ring. The invention further provides novel Echinocandin type compounds and their use as antifungal or anti-parasitic agents.</p>		

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INTERNATIONAL SEARCH REPORT

Intern. Application No
PCT/US 99/18908

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K7/50 A61K38/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>NATSUKO KUROKAWA ET AL: "SYNTHETIC STUDIES ON ANTIFUNGAL CYCLIC PEPTIDES, ECHINOCANDINS. STEREOSELECTIVE TOTAL SYNTHESIS OF ECHINOCANDIN D VIA A NOVAL PEPTIDE COUPLING"</p> <p>TETRAHEDRON, NL, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, vol. 49, no. 28, page 6195-7022 XP000571478</p> <p>ISSN: 0040-4020</p> <p>cited in the application</p> <p>the whole document</p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/--</p>	1-11

☒ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

* Special categories of cited documents :

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"E" earlier document but published on or after the international filing date

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"P" document published prior to the international filing date but later than the priority date claimed

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"A" document member of the same patent family

Date of the actual completion of the international search

23 December 1999

Date of mailing of the international search report

12 04 2000

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

Inten. nal Application No
PCT/US 99/18908

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>HENSENS E.A.: "Pneumocandins from Zalerion arboricola" JOURNAL OF ANTIBIOTICS., vol. 45, no. 12, XP002126647 JAPAN ANTIBIOTICS RESEARCH ASSOCIATION. TOKYO., JP ISSN: 0021-8820 See especially pages 180-1882 ---</p>	1-11
A	<p>JAMISON E.A.: "The synthesis and antifungal activity of nitrogen containing hemiaminal ethers of LY303366" JOURNAL OF ANTIBIOTICS., vol. 51, no. 2, February 1998 (1998-02), pages 239-242, XP002126600 JAPAN ANTIBIOTICS RESEARCH ASSOCIATION. TOKYO., JP ISSN: 0021-8820 See especially page 239, introduction ---</p>	1-11
A	<p>ZAMBIAS E.A.: "Preparation and structure-activity ewlationships of simplified analogues of the antifungal agent cilofungin: a total synthesis approach" JOURNAL OF MEDICINAL CHEMISTRY, vol. 35, no. 15, 1992, pages 2843-2855, XP002126648 WASHINGTON US cited in the application the whole document -----</p>	1-11

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/ 18908

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 17-20 encompass or are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-11

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-11

Process for modifying a cyclic peptide ring nucleus.

2. Claims: 12-20

Compounds as defined in claim 12 and their use.